An Observational Analysis of Clinical Presentation and Prognosis in Pregnancy-Related Cerebral Venous Sinus Thrombosis

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Background: *Cerebral venous sinus thrombosis (CVST) represents an uncommon yet severe vascular complication associated with pregnancy and the puerperium, presenting with diverse clinical manifestations. Limited data are available regarding its prognostic indicators during the acute phase, as well as outcomes of subsequent pregnancies and recurrence risk. This study aimed to evaluate the clinical characteristics and prognosis of pregnancy-related CVST in a Chinese population.*

Methods: *Clinical records of 41 women diagnosed with CVST during pregnancy or the puerperal period between January 2007 and March 2018 at Shengjing Hospital were retrospectively reviewed. A poor outcome was defined as a modified Rankin Scale (mRS) score ≥3 at discharge. Independent prognostic factors were determined using multivariate logistic regression analysis. Follow-up outpatient interviews were conducted to assess future pregnancy outcomes and CVST recurrence.*

Results: *The incidence of CVST was approximately 2.4 times higher during the puerperium (29 cases) compared to pregnancy (12 cases). Headache was the most frequent presenting symptom (90%), followed by focal neurological deficits (61%), seizures (59%), visual disturbances (37%), and altered consciousness (29%). Multivariate analysis identified elevated D-dimer levels (>1134 μg/L; OR=18.67, 95% CI: 1.79–194.84) and impaired consciousness (OR=33.85, 95% CI: 3.14–365.45) as independent predictors of poor outcomes during the acute phase. Long-term follow-up was completed for 28 patients (68%). Three women experienced multiple pregnancies (six in total), though none resulted in childbirth. One patient experienced CVST recurrence three years later, unrelated to pregnancy or puerperium.*

Conclusions: *CVST occurred predominantly during the puerperium. Elevated D-dimer levels above 1134 μg/L and impaired consciousness were strong indicators of poor prognosis. The rates of subsequent pregnancy and CVST recurrence were low among this cohort of Chinese women.*

BACKGROUND

Cerebral venous sinus thrombosis (CVST) is an uncommon form of cerebrovascular disorder, representing approximately 0.5% of all stroke cases [1]. Among the various etiologies, pregnancy and the puerperal period are recognized as major risk factors because of the distinct physiological and hemostatic changes occurring during these stages [2,3]. Women who are pregnant have nearly a threefold higher risk of developing CVST compared with non-pregnant women of reproductive age[4]. The reported incidence of pregnancy-associated CVST varies widely, ranging from 8.9 to 450 cases per 100,000 deliveries annually[5–9], with maternal mortality rates reported as high as 9–18.5%[3,8,10]. Such outcomes carry serious implications for both affected families and public health systems.

Early recognition and appropriate management of CVST are crucial to minimize disability and

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mortality. However, the clinical presentation of pregnancy-related CVST is often diverse—ranging from mild headache to profound coma—and can mimic other pregnancy-related neurological disorders, including eclampsia, reversible cerebral vasoconstriction syndrome (RCVS), and posterior reversible encephalopathy syndrome (PRES)[11].

Despite increasing awareness, data regarding prognostic factors during the acute phase of CVST, as well as the impact on future pregnancies and recurrence risk, remain limited. Hence, the present study aims to comprehensively analyze the clinical characteristics of pregnancy-associated CVST, determine independent predictors of poor outcomes during the acute phase, and assess its influence on subsequent pregnancy outcomes and recurrence rates.

MATERIALS AND METHODS

Patient Selection

A retrospective review was conducted on women diagnosed with cerebral venous sinus thrombosis (CVST) during pregnancy or the puerperal period at Shengjing Hospital, China Medical University, between January 2007 and March 2018. The study protocol was approved by the Ethics Committee of the University Hospital.

(1) Patients were included if they met the following criteria:(2) Age between 18 and 45 years; (3) Onset of CVST during pregnancy or within six weeks postpartum Radiologically confirmed diagnosis of CVST by magnetic resonance imaging/venography (MRI/MRV) or digital subtraction angiography (DSA); (4) No prior history of venous thromboembolism or relevant hereditary thrombophilia.

Individuals were excluded if they had a known history of seizures, malignancy, hematologic disorders, inflammatory bowel disease, nephrotic syndrome, or connective tissue diseases.

Clinical Variables

Clinical and laboratory information was collected and analyzed across seven major domains:

(1) Baseline demographics: including age at CVST onset, number of pregnancies, duration from symptom onset to hospital admission (categorized as acute <48 hours, subacute 48 hours–30 days, or chronic >30 days), and time from symptom onset to initiation of treatment. (2) Risk factors: presence of comorbid conditions such as hypertension, diabetes mellitus, hyperlipidemia, smoking, or alcohol consumption. (3) Clinical presentation: primary symptoms including headache, seizures, focal neurological deficits (motor or sensory impairment, or aphasia), visual disturbances (e.g., blurred vision, hemianopia, visual neglect, or cortical blindness), and altered level of consciousness. (4) Laboratory and imaging findings: results obtained within 24 hours of hospital admission, including D-dimer levels measured via immunoturbidimetric assay using an automated coagulation analyzer (reference range: 0–252 μg/L), and neuroimaging findings on MRI/MRV or DSA. (5) Treatment: therapeutic interventions received during hospitalization and post-discharge. (6) Functional outcome: assessed using the modified Rankin Scale (mRS) at discharge, independently evaluated by two neurologists. A poor outcome was defined as an mRS score ≥3. (7) Follow-up information: collected on subsequent pregnancy outcomes and recurrence of CVST.

Statistical Analysis

Continuous data were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on data distribution, while categorical data were reported as frequencies and percentages. Comparisons between groups were performed using the Student's t-test or Mann–Whitney U test for continuous variables, and Pearson's χ^2 test or Fisher's exact test for categorical variables.

Variables with a p value <0.20 in univariate analysis were entered into a multivariate logistic regression model using a forward selection approach. Model fit was evaluated by the Hosmer–Lemeshow goodness-of-fit test. The receiver operating characteristic (ROC) curve was used to determine the optimal D-dimer cut-off value predictive of poor outcomes in the acute phase

of CVST.

All statistical analyses were carried out using SPSS software, version 21.0 (IBM Corp., Armonk, NY, USA). A two-tailed p value <0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

A total of 41 patients met the inclusion criteria for this study. The baseline clinical characteristics are summarized in Table 1. The mean age at onset was 29.7 ± 5.9 years. All patients presented with either acute or subacute disease onset, and the median hospital stay was 23 days (IQR: 10.5–33.5). Among these, 29 women (71%) developed CVST during the puerperium, which was approximately 2.4 times more frequent than during pregnancy (12 cases). The average interval between delivery and symptom onset was eight days, ranging from 1 to 40 days. During pregnancy, CVST most commonly occurred in the first and second trimesters. Only two patients had a history of chronic hypertension prior to pregnancy, and none had diabetes mellitus, cardiac disorders, smoking, or alcohol use. Among pregnancy-related complications, 13 patients (32%) were diagnosed with gestational hypertension, 11 (27%) with preeclampsia, and 4 (10%) with eclampsia at the time of CVST diagnosis.

Clinical Presentations, Laboratory Findings, and Neuroimaging

The most frequent symptom was headache, reported in 37 patients (90%), followed by focal neurological deficits in 25 (61%), seizures in 24 (59%), visual disturbances in 15 (37%), and impaired consciousness in 12 (29%) (Table 1). Laboratory testing revealed hyperlipidemia in 21 patients (66%), hypoproteinemia in 20 (49%), anemia in 19 (46%), and HELLP syndrome in 3 (7%). The median D-dimer concentration was 1001 μg/L (IQR: 715–2486.5 μg/L), though three patients had values below 500 μg/L.

Neuroimaging confirmed CVST via MRI/MRV in 40 patients and DSA in one patient. Venous infarction was observed in 28 cases (68%), while intracerebral hemorrhage was identified in 23 (56%). The parietal lobe was the most frequently affected region (21 patients, 51%), followed by the frontal lobe (12, 29%), occipital lobe (10, 24%), temporal lobe (5, 12%), basal ganglia (3, 7%), and cerebellum (2, 5%).

Magnetic resonance venography demonstrated that the sigmoid sinus (24, 59%), transverse sinus (22, 54%), and superior sagittal sinus (21, 51%) were the most commonly involved venous structures. More than one sinus was affected in 26 patients (63%).

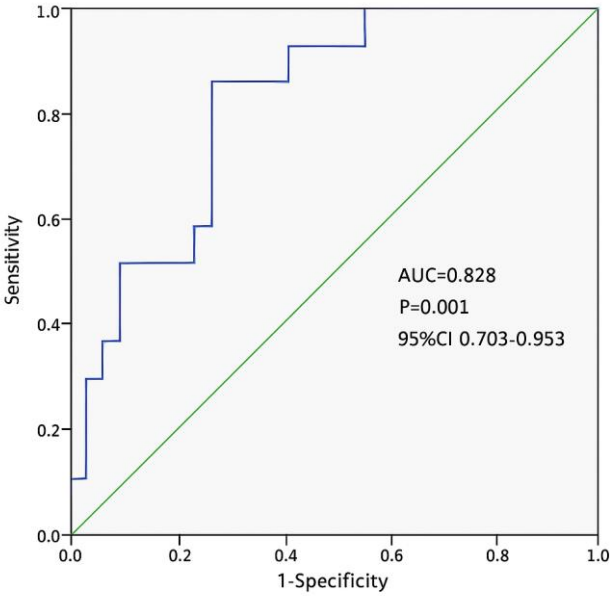
Treatment and Outcomes at Discharge

All patients received symptomatic therapy, including management of seizures, intracranial hypertension, and elevated blood pressure. Anticoagulation with low-molecular-weight heparin (LMWH) was initiated promptly after diagnosis in 37 patients and continued for approximately two weeks, followed by oral anticoagulant therapy after discharge. Four patients did not receive anticoagulation due to the presence of significant intracerebral hemorrhage. One of these patients underwent surgical intervention for brain midline shift. At discharge, patients were categorized based on their modified Rankin Scale (mRS) scores. Twenty-seven patients (66%) achieved a good outcome (mRS ≤ 2), while fourteen (34%) had poor outcomes (mRS ≥ 3), including two in-hospital deaths. Baseline characteristics of both groups are presented in Table 2.

Univariate analysis identified several factors associated with poor outcome, including gestational hypertension, preeclampsia, eclampsia, headache, focal neurological deficits, intracerebral hemorrhage, impaired consciousness, elevated D-dimer levels, and lack of anticoagulation ($p < 0.2$).

Receiver operating characteristic (ROC) curve analysis demonstrated that D-dimer levels significantly predicted poor outcomes, with an area under the curve (AUC) of 0.828 (95% CI: 0.703–0.953; $p = 0.001$). The optimal D-dimer cut-off value was 1134 μg/L, yielding 85.7% sensitivity and 74.1% specificity (Figure 1).

Figure 1: Receiver operating characteristic (ROC) curve demonstrating the predictive value of D-dimer levels for poor outcomes in cerebral venous thrombosis (CVT) occurring during pregnancy and the puerperium.



AUC: area under the curve; CI: confidence interval.

Univariate analysis showed that D-dimer levels >1134 μg/L were strongly associated with poor outcomes (26% vs. 86%; $p < 0.001$). In multivariate logistic regression, D-dimer >1134 μg/L (OR = 18.67, 95% CI: 1.79–194.84) and impaired consciousness (OR = 33.85, 95% CI: 3.14–365.45) emerged as independent predictors of poor prognosis. Model calibration by the Hosmer–Lemeshow test indicated a good fit ($p = 0.513$) (Table 3).

Long-Term Follow-Up

Twenty-eight patients (68%) completed long-term follow-up, with a median duration of 3.5 years (range: 0.3–8.4 years). Among them, 25 (89%) recovered completely without residual deficits, one experienced persistent visual impairment, and two remained severely disabled (mRS = 4). A majority of women (22, 79%) expressed fear of subsequent pregnancies due to concerns about CVST recurrence. Only three women experienced multiple pregnancies (six total, two each), but none resulted in live births. Two patients elected for termination of early pregnancies because of recurrence anxiety, while one experienced two miscarriages due to low progesterone levels. Only one patient developed a recurrent CVST episode three years after the initial event, with no identified pregnancy or puerperal association or other specific cause.

Table 1: Demographic, clinical, laboratory, and neuroimaging findings of patients with cerebral venous thrombosis (CVT)

Characteristics	Data
Age (years)	29.7 ± 5.9
Multiple pregnancy (n = 2)	20 (49%)
Mode of onset	
Acute	17 (41%)
Subacute	24 (59%)
Pregnancy period	
First trimester	5 (12%)
Second trimester	5 (12%)
Third trimester	2 (5%)
Puerperium	29 (71%)
Hypertension	2 (5%)
Gestational hypertension	13 (32%)

Preeclampsia	**11 (27%)**
Eclampsia	4 (10%)
Initial symptoms	
Headache	37 (90%)
Focal neurological deficits	25 (61%)
Epileptic seizures	24 (59%)
Visual disturbance	15 (37%)
Impaired consciousness	12 (29%)
Laboratory findings	
Hyperlipidemia*	21 (66%)
Hypoproteinemia†	20 (49%)
Anemia‡	19 (46%)
HELLP syndrome§	3 (7%)
D-dimer (μg/L)	1001 (715, 2486.5)
Neuroimaging findings	
Infarction	28 (68%)
Hemorrhage	23 (56%)
Sigmoid sinus involvement	24 (59%)
Transverse sinus involvement	22 (54%)
Superior sagittal sinus involvement	21 (51%)
Inferior sagittal/straight sinus involvement	7 (17%)
Multiple sinus involvement (n = 2)	26 (63%)

Notes:
Missing data (N = 9); a total of 32 patients underwent lipid testing.
† Albumin < 25 g/L or total protein < 60 g/L.
‡ Hemoglobin concentration < 110 g/L during pregnancy.
§ HELLP: hemolysis, elevated liver enzymes, and low platelet count.

Table 2: Univariate analysis of prognostic factors associated with functional outcome at discharge in patients with cerebral venous thrombosis (CVT)

Variable	Favorable outcome (mRS ≤ 2, n = 27)	Poor outcome (mRS ≥ 3, n = 14)	p-value
Age (years, Mean ± SD)	29.4 ± 6.0	30.4 ± 5.8	0.618
Multiple pregnancy	13/27 (48%)	7/14 (50%)	0.91
Gestational hypertension	5/27 (19%)	8/14 (57%)	0.03
Preeclampsia	5/27 (19%)	6/14 (43%)	0.195
Eclampsia	1/27 (4%)	3/14 (21%)	0.107
Systolic blood pressure (mmHg)	132.4 ± 26.8	143.6 ± 32.9	0.249

Diastolic blood pressure (mmHg)	**85.3 ± 19.3**	**92.9 ± 22.1**	**0.262**
Puerperium	21/27 (78%)	8/14 (57%)	0.31
Headache	26/27 (96%)	11/14 (79%)	0.107
Seizures	15/27 (56%)	9/14 (64%)	0.591
Visual disturbance	9/27 (33%)	6/14 (43%)	0.548
Focal neurological deficits	13/27 (48%)	12/14 (86%)	0.019
Impaired consciousness	2/27 (7%)	10/14 (71%)	< 0.001
Hyperlipidemia*	15/24 (63%)	6/8 (75%)	0.83
Anemia	11/27 (41%)	8/14 (57%)	0.318
Hypoproteinemia	14/27 (52%)	6/14 (43%)	0.585
HELLP syndrome	1/27 (4%)	2/14 (14%)	0.265
D-dimer (μg/L)	800 (692, 1541)	2186.5 (1177, 5492)	0.001
Intracerebral hemorrhage	11/27 (41%)	12/14 (86%)	0.006
Multiple sinus involvement (n = 2)	17/27 (63%)	9/14 (64%)	0.934
Anticoagulation therapy	26/27 (96%)	11/14 (79%)	0.107

Notes:

- Missing data (N = 9); a total of 32 patients underwent lipid testing.
- mRS – modified Rankin Scale; SD – standard deviation.
- $p < 0.05$ considered statistically significant. *

Table 3: Independent predictors of poor outcome in cerebral venous thrombosis (CVT) during pregnancy and puerperium

Variable	Exp(B)	95% Confidence Interval	p-value
D-dimer > 1134 μg/L	18.67	1.79 – 194.83	0.014
Impaired consciousness	33.85	3.14 – 365.45	0.004

DISCUSSION

Pregnancy and the postpartum period are well-recognized as high-risk phases for the development of cerebral venous sinus thrombosis (CVST), primarily due to physiological changes such as hypercoagulability, venous stasis, and endothelial dysfunction[12,13]. In agreement with previous literature, our findings demonstrated that the incidence of CVST was significantly higher during the puerperal period than during pregnancy [10,11]. Several factors may contribute to this increased risk, including postpartum hemorrhage, dehydration, anemia, infection, and prolonged immobilization following delivery[7,11–13]. The clinical presentation of CVST is notably diverse and largely depends on the extent of sinus involvement, the presence of collateral circulation, and the resulting intracranial pressure alterations[14]. Headache is the most frequently reported symptom, occurring in 60–90% of patients[15].

Similarly, in our study, headache was the predominant manifestation, present in 90% of cases, with four patients experiencing isolated headache as the only symptom. While headache is common in

normal pregnancy and the puerperium, certain features—such as thunderclap onset, a new or changing headache pattern, or association with elevated blood pressure—should raise clinical suspicion for CVST[11].

Physiological alterations during pregnancy, including hyperlipidemia, anemia, and hypoproteinemia, were frequently observed but did not influence clinical outcomes in our cohort. In line with prior studies, the sigmoid, transverse, and superior sagittal sinuses were the most commonly affected venous structures[16,17]. Previous studies have suggested that pregnancy-related CVST generally has a more favorable prognosis compared with other etiologies of CVST[3] and is associated with better outcomes than pregnancy-related ischemic or hemorrhagic stroke[10,16]. While several prognostic indicators have been identified in the general CVST population—such as coma, intracerebral hemorrhage (ICH), seizures, older age, and neurological deficits [17,18]—prognostic factors specific to pregnancy-related CVST remain insufficiently defined.

In the present study, multivariate analysis identified elevated D-dimer levels (>1134 μg/L) and impaired consciousness as independent predictors of poor outcome. D-dimer, a fibrin degradation product, serves as a biomarker of hypercoagulability and has been shown to correlate with the extent and severity of thrombosis[19–21]. Hence, D-dimer monitoring may provide valuable insight into disease severity and prognosis in CVST. Although preeclampsia and eclampsia are leading causes of ischemic and hemorrhagic stroke in pregnancy, their role in CVST appears limited[10]. Our analysis similarly found no significant relationship between these conditions and outcomes of pregnancy-related CVST.

Low-molecular-weight heparin (LMWH) remains the treatment of choice for CVST, including cases complicated by ICH[22]. The optimal duration of anticoagulation is not firmly established; however, the American Heart Association/American Stroke Association (AHA/ASA) guidelines recommend LMWH throughout pregnancy and continuation with either LMWH or vitamin K antagonists (target INR 2–3) for at least six months postpartum [22,23]. Endovascular thrombolysis may be considered for patients with poor response or deteriorating neurological status[18]. To our knowledge, this is the first study to report on the recurrence of pregnancy-associated CVST in a Chinese population. Prior research has primarily examined CVST recurrence among women of childbearing age[24]. observed no recurrence among 22 pregnancies and 19 live births in 14 women with a prior CVST episode, while[25] identified a recurrence rate of 8 per 1,000 individuals (95% CI: 3–22) in a systematic review.

Our long-term follow-up findings revealed that most women avoided subsequent pregnancies due to fear of recurrence. Only three women conceived again (six pregnancies in total), none resulting in live births—two terminated early pregnancies by choice, and one experienced two miscarriages linked to low progesterone levels. Only one patient (3.5%) experienced a recurrent CVST, which was not pregnancy-related. Available evidence suggests that the recurrence risk of venous thromboembolism (VTE), including CVST, is low when the initial event is associated with a transient risk factor, such as oral contraceptive use or immobilization[24,26]. Conversely, risk increases in the presence of inherited thrombophilia or idiopathic thrombosis[7,11,24]. Therefore, women with a history of CVST should undergo thrombophilia screening and minimize exposure to modifiable risk factors before future pregnancies. Prophylactic LMWH may also be beneficial during subsequent pregnancies to reduce recurrence risk[25,27].

LIMITATIONS

This study has several limitations that should be acknowledged. First, it was a retrospective analysis conducted at a single tertiary care center, which may limit the generalizability of the findings to broader populations. Second, genetic factors predisposing to thrombosis—such as mutations in the methylenetetrahydrofolate reductase (MTHFR) gene or Factor V Leiden—were not evaluated. Nevertheless, none of the patients had a prior history of thrombotic events or a known family history of thrombophilia, suggesting that these genetic factors were unlikely to have influenced the study outcomes.

CONCLUSIONS

In summary, cerebral venous sinus thrombosis (CVST) is an uncommon but potentially life-threatening complication during pregnancy and the puerperium. In this cohort, elevated D-dimer levels exceeding 1134 μg/L and impaired consciousness at presentation were identified as independent predictors of poor prognosis. The incidence of subsequent pregnancies and CVST recurrence was low among affected women in this Chinese population. Future large-scale, multicenter studies are warranted to further elucidate the prognostic factors and long-term outcomes of pregnancy-related CVST, thereby improving evidence-based counseling and management strategies for these patients.

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